

MEANS AND METHOD FOR GUIDING
IONS IN A MASS SPECTROMETER

1 TECHNICAL FIELD OF THE INVENTION

2 The present invention relates to a method and apparatus for
3 the injection of ions into a mass spectrometer for subsequent
4 analysis. An apparatus for use in an ion source having an ion
5 production means and an ion guide is described which facilitates
6 the transmission of ions from an elevated pressure ion production
7 region to a reduced pressure ion analysis region of a mass
8 spectrometer for mass analysis. Specifically, a preferred
9 embodiment of the present invention allows a multitude of ion
10 production means to simultaneously introduce ions into a single ion
11 guide and transmit the ions to a mass analyzer.

12
13 BACKGROUND OF THE PRESENT INVENTION

14 The present invention relates to multipole ion guides for use
15 in mass spectrometry. The apparatus and methods for ionization
16 described herein are enhancements of the techniques that are
17 referred to in the literature relating to mass spectrometry -- an
18 important tool in the analysis of a wide range of chemical
19 compounds. Specifically, mass spectrometers can be used to
20 determine the molecular weight of sample compounds. The analysis
21 of samples by mass spectrometry consists of three main steps --

1 formation of gas phase ions from sample material, mass analysis of
2 the ions to separate the ions from one another according to ion
3 mass, and detection of the ions. A variety of means and methods
4 exist in the field of mass spectrometry to perform each of these
5 three functions. The particular combination of the means and
6 methods used in a given mass spectrometer determine the
7 characteristics of that instrument.

8 To mass analyze ions, for example, one might use magnetic (B)
9 or electrostatic (E) analysis. Ions passing through a magnetic or
10 electrostatic field will follow a curved path. In a magnetic field
11 the curvature of the path will be indicative of the momentum-to-
12 charge ratio of the ion. In an electrostatic field, the curvature
13 of the path will be indicative of the energy-to-charge ratio of the
14 ion. If magnetic and electrostatic analyzers are used
15 consecutively, then both the momentum-to-charge and energy-to-
16 charge ratios of the ions will be known and the mass of the ion
17 will thereby be determined. Other mass analyzers are the
18 quadrupole (Q), the ion cyclotron resonance (ICR), the time-of-
19 flight (TOF), and the quadrupole ion trap analyzers. The analyzer
20 which accepts ions from the ion guide described here may be any of
21 a variety of these.

22 Before mass analysis can begin, however, gas phase ions must
23 be formed from sample material. If the sample material is

1 sufficiently volatile, ions may be formed by electron ionization
2 (EI) or chemical ionization (CI) of the gas phase sample molecules.
3 For solid samples (e.g., semiconductors, or crystallized
4 materials), ions can be formed by desorption and ionization of
5 sample molecules by bombardment with high energy particles.
6 Secondary ion mass spectrometry (SIMS), for example, uses keV ions
7 to desorb and ionize sample material. In the SIMS process a large
8 amount of energy is deposited in the analyte molecules. As a
9 result, fragile molecules will be fragmented. This fragmentation
10 is undesirable in that information regarding the original
11 composition of the sample (e.g., the molecular weight of sample
12 molecules) will be lost.

13 For more labile, fragile molecules, other ionization methods
14 now exist. The plasma desorption (PD) technique was introduced by
15 Macfarlane et al. in 1974 (Macfarlane, R. D.; Skowronski, R. P.;
16 Torgerson, D. F., *Biochem. Biophys. Res Commun.* **60** (1974) 616).
17 Macfarlane et al. discovered that the impact of high energy (MeV)
18 ions on a surface, like SIMS would cause desorption and ionization
19 of small analyte molecules. However, unlike SIMS, the PD process
20 results also in the desorption of larger, more labile species
21 (e.g., insulin and other protein molecules).

22 Lasers have been used in a similar manner to induce desorption
23 of biological or other labile molecules. See, for example,

1 VanBreeman, R.B.: Snow, M.: Cotter, R.J., *Int. J. Mass Spectrom.*
2 *Ion Phys.* **49** (1983) 35; Tabet, J.C.; Cotter, R.J., *Anal. Chem.* **56**
3 (1984) 1662; or Olthoff, J.K.; Lys, I.: Demirev, P.: Cotter, R.
4 J., *Anal. Instrument.* **16** (1987) 93. Cotter et al. modified a CVC
5 2000 time-of-flight mass spectrometer for infrared laser desorption
6 of involatile biomolecules, using a Tachisto (Needham, Mass.)
7 model 215G pulsed carbon dioxide laser. The plasma or laser
8 desorption and ionization of labile molecules relies on the
9 deposition of little or no energy in the analyte molecules of
10 interest. The use of lasers to desorb and ionize labile molecules
11 intact was enhanced by the introduction of matrix assisted laser
12 desorption ionization (MALDI) (Tanaka, K.; Waki, H.; Ido, Y.;
13 Akita, S.; Yoshida, Y.; Yoshida, T., *Rapid Commun. Mass Spectrom.*
14 **2** (1988) 151 and Karas, M.; Hillenkamp, F., *Anal. Chem.* **60** (1988)
15 2299). In the MALDI process, an analyte is dissolved in a solid,
16 organic matrix. Laser light of a wavelength that is absorbed by
17 the solid matrix but not by the analyte is used to excite the
18 sample. Thus, the matrix is excited directly by the laser, and the
19 excited matrix sublimates into the gas phase carrying with it the
20 analyte molecules. The analyte molecules are then ionized by
21 proton, electron, or cation transfer from the matrix molecules to
22 the analyte molecules. This process, MALDI, is typically used in
23 conjunction with time-of-flight mass spectrometry (TOFMS) and can

1 be used to measure the molecular weights of proteins in excess of
2 100,000 daltons.

3 Atmospheric pressure ionization (API) includes a number of
4 methods. Typically, analyte ions are produced from liquid solution
5 at atmospheric pressure. One of the more widely used methods,
6 known as electrospray ionization (ESI), was first suggested by Dole
7 et al. (M. Dole, L.L. Mack, R.L. Hines, R.C. Mobley, L.D. Ferguson,
8 M.B. Alice, *J. Chem. Phys.* **49**, 2240, 1968). In the electrospray
9 technique, analyte is dissolved in a liquid solution and sprayed
10 from a needle. The spray is induced by the application of a
11 potential difference between the needle and a counter electrode.
12 The spray results in the formation of fine, charged droplets of
13 solution containing analyte molecules. In the gas phase, the
14 solvent evaporates leaving behind charged, gas phase, analyte ions.
15 Very large ions can be formed in this way. Ions as large as 1 MDa
16 have been detected by ESI in conjunction with mass spectrometry
17 (ESMS).

18 For example, FIG. 1 depicts a conventional mass spectrometer
19 using an ESI ion source. As shown, ions are introduced into
20 ionization chamber via spray needle 10. At the end of spray needle
21 10, the solution is formed into a spray 12 of fine droplets. Spray
22 12 is formed as a result of an electrostatic field applied between
23 spray needle 10 and sampling orifice 14. Sampling orifice 14 may

1 be an aperture, capillary (shown), or other similar inlet leading
2 into vacuum chamber 4 of the mass spectrometer. While in the
3 ionization chamber 2, electrosprayed droplets evaporate thereby
4 producing gas phase analyte ions. In addition, heated drying gas
5 may be used to assist the evaporation of the droplets. The analyte
6 ions are carried with the gas from ionization chamber 2 through the
7 sampling orifice 14 and into the differential pumping system of the
8 mass spectrometer, comprising vacuum chambers 4, 6 & 8 and pumps
9 20, 22, & 24. With the assistance of electrostatic lens 16 and a
10 conventional ion guide 18, sample analyte ions pass through the
11 vacuum system of the source (i.e., regions 4 & 6) before entering
12 high vacuum region 8 wherein the mass analyzer (not shown) is
13 positioned. Once in the mass analyzer, the sample ions are
14 analyzed to produce a mass spectrum. Some of the analyzers which
15 may be used in such a system include quadrupole, ICR, TOF, etc.

16 In addition to ESI, any other ion production method that can
17 be adapted to atmospheric pressure might be used. For example,
18 MALDI has recently been adapted by Victor Laiko and Alma Burlingame
19 to work at atmospheric pressure (Atmospheric Pressure Matrix
20 Assisted Laser Desorption Ionization, poster #1121, 4th
21 International Symposium on Mass Spectrometry in the Health and Life
22 Sciences, San Francisco, Aug. 25 - 29, 1998) and by Standing et al.
23 at elevated pressures (Time of Flight Mass Spectrometry of

1 Biomolecules with Orthogonal Injection + Collisional Cooling,
2 poster #1272, 4th International Symposium on Mass Spectrometry in
3 the Health and Life Sciences, San Francisco, Aug. 25 - 29, 1998;
4 and Orthogonal Injection TOFMS *Anal. Chem.* 71(13), 452A (1999)).
5 The benefit of adapting ion sources in this manner is that the ion
6 optics and mass spectral results are largely independent of the ion
7 production method used.

8 An elevated pressure ion source always has an ion production
9 region (wherein ions are produced) and an ion transfer region
10 (wherein ions are transferred through differential pumping stages
11 and into the mass analyzer). The ion production region is at an
12 elevated pressure -- most often atmospheric pressure -- with
13 respect to the analyzer. The ion production region will often
14 include an ionization "chamber" (e.g. FIG. 1, ionization chamber
15 4). In an ESI source, for example, liquid samples are "sprayed"
16 into the "chamber" to form ions.

17 Once the ions are produced, they must be transported to the
18 vacuum for mass analysis. Generally, mass spectrometers (MS)
19 operate in a vacuum between 10^{-4} and 10^{-10} torr depending on the
20 type of mass analyzer used. In order for the gas phase ions to
21 enter the mass analyzer, they must be separated from the background
22 gas carrying the ions and transported through the single or
23 multiple vacuum stages.

1 The use of multipole ion guides has been shown to be an
2 effective means of transporting ions through a vacuum system.
3 Publications by Olivers et al. (Anal. Chem, Vol. 59, p. 1230-1232,
4 1987), Smith et al. (Anal. Chem. Vol. 60, p. 436-441, 1988) and
5 Douglas et al. U.S. Pat. No. 4,963,736 (Douglas) have reported the
6 use of AC-only quadrupole ion guides to transport ions from an API
7 source to a mass analyzer. Such multipole ion guides may be
8 configured as collision cells capable of being operated in RF only
9 mode with a variable DC offset potential applied to all rods.
10 Thomson et al., U.S. Patent Number 5,847,386 (Thomson) also
11 describes a quadrupole ion guide. The ion guide of Thomson is
12 configured to create a DC axial field along its axis to move ions
13 axially through a collision cell, *inter alia*, or to promote
14 dissociation of ions (i.e., by Collision Induced Dissociation
15 (CID)).

16 Other schemes are available utilizing both RF and DC
17 potentials in order to facilitate the transmission of ions of a
18 certain range of m/z values. For example, in H.R. Morris et al.,
19 High Sensitivity Collisionally Activated Decomposition Tandem Mass
20 Spectrometry on a Novel Quadrupole/ Orthogonal Acceleration Time-
21 of-Flight Mass Spectrometer, *Rapid Commun. Mass Spectrom.* 10, 889
22 (1996) (Morris), uses a series of multipoles in their design, one of
23 which is a quadrupole which is capable of being operated in a "wide

1 bandpass" mode or a "narrow bandpass" mode. In the wide bandpass
2 mode, an RF-only potential is applied to the quadrupole and ions of
3 a relatively broad range of m/z values are transmitted. In narrow
4 bandpass mode both RF and DC potentials are applied to the
5 quadrupole such that ions of only a narrow range of m/z values are
6 selected for transmission through the quadrupole. In subsequent
7 multipoles the selected ions may be activated towards dissociation.
8 In this way, the instrument of Morris is able to perform MS/MS
9 experiments with the first mass analysis and subsequent
10 fragmentation occurring in what would otherwise be simply a set of
11 multipole ion guides.

12 Further, mass spectrometers similar to that of Whitehouse et
13 al. U.S. Patent No. 5,652,427 (Whitehouse), entitled "Multipole Ion
14 Guide for Mass Spectrometry", use multipole RF ion guides to
15 transfer ions from one pressure region to another in a
16 differentially pumped system. In the source of Whitehouse, ions
17 are produced by ESI or APCI at substantially atmospheric pressure.
18 These ions are transferred from atmospheric pressure to a first
19 differential pumping region by the gas flow through a glass
20 capillary. Ions are transferred from this first pumping region to
21 a second pumping region through a "skimmer" by an electric field
22 between these regions as well as gas flow. A multipole in the
23 second differentially pumped region accepts ions and guides them

1 through a restriction and into a third differentially pumped
2 region. This is accomplished by applying AC and DC voltages to the
3 individual poles.

4 A four vacuum stage ES/MS quadrupole mass spectrometer
5 according to Whitehouse, incorporating a multipole ion guide
6 beginning in one vacuum pumping stage and extending contiguously
7 into an adjacent pumping stage, is depicted in FIG. 2. As
8 discussed above, ions are formed from sample solution by an
9 electrospray process when a potential is applied between spray
10 needle 27 of sprayer 26 and sampling orifice 38. According to the
11 prior art system shown in FIG. 2, capillary 60 is used to transport
12 ions from atmospheric pressure region 28, where the ions are
13 formed, to first pumping region 30. Lenses 62 and 56 are used to
14 guide the ions from exit end 40 of capillary 60 to a fourth pumping
15 region 36 containing a mass analyzer. In this case, a reflectron
16 TOF mass analyzer is shown. Between lenses 62 and 48, RF only
17 hexapole ion guide 42 is used to guide ions through differential
18 pumping stages 32 and 34 to exit end 46 of ion guide 42 and into
19 mass analysis region 36 through orifice 50. The hexapole ion guide
20 42 according to this prior art design is intended to provide for
21 the efficient transport of ions from one location (i.e., the
22 entrance 58 of skimmer 56) to a second location (i.e., orifice 50).
23 FIG. 2 is a diagram of a four vacuum pumping stage orthogonal

1 pulsing API/MS system with a reflectron Time-Of-Flight mass
2 analyzer. For the purpose of illustration, an electrospray ion
3 source is shown as the API source. This could alternatively be an
4 APCI or an ICP source. Sample bearing liquid is introduced through
5 the electrospray needle 26 and is electrosprayed (with or without
6 pneumatic assistance) into chamber 28 as it exits the needle at 27.
7 The charged droplets produced evaporate and desorb gas phase ions
8 both in chamber 28 and as they are swept into the vacuum of a mass
9 spectrometer through the annulus in capillary 60. A portion of the
10 ions that enter the first vacuum stage 30 through the capillary
11 exit 40 are focused through the orifice 58 in skimmer 56 with the
12 help of lens 62 and the potential set on the capillary exit 40.
13 Ions passing through skimmer orifice 58 enter the multipole ion
14 guide 42 which begins in vacuum pumping stage 32 and extends
15 unbroken into vacuum stage 34. If the multipole ion guide AC and
16 DC voltages are set to pass ions falling within a range of m/z then
17 ions within that range which enter the multipole ion guide will
18 exit at 46 and are focused with exit lens 48 through the TOF
19 analyzer entrance orifice 50. This primary ion beam 82 passes
20 between electrostatic lenses 64 and 68 located in the fourth
21 pumping stage 36. The relative voltages on lenses 64, 68 and 70
22 are pulsed so that a portion of the ion beam 82 falling in between
23 lenses 64 and 68 is ejected as a packet through grid lens 70 and

1 accelerated down flight tube 80. The ions are steered by x and y
2 lens sets diagrammatically illustrated by 72 as they continue
3 moving down flight tube 80. As shown in this illustrative
4 configuration, the ion packet is reflected through a reflectron or
5 ion mirror 78 and detected at detector 74. As a pulsed ion packet
6 proceeds down flight tube 80, ions with different m/z separate in
7 space due to their velocity differences and arrive at the detector
8 at different times. The use of orthogonal pulsing in an API/TOF
9 system helps to reduce the ion energy spread of the initial ion
10 packet allowing for the achievement of higher resolution and
11 sensitivity. Also disclosed by Whitehouse is the use of
12 collisional gas within hexapole ion guide 42 to cool the ions to
13 thermal velocities through collisional cooling.

14 In the scheme of Whitehouse, an RF only potential is applied
15 to multipole ion guide 42. As a result, ion guide 42 is not
16 "selective" but rather transmits ions over a broad range of mass-
17 to-charge (m/z) ratios. Such a range as provided by prior art
18 multipoles is inadequate for certain applications, such as for
19 Matrix Assisted Laser Desorption/Ionization (MALDI), because the
20 ions produced may be well out of this m/z range. In other words,
21 high m/z ions such as are often produced by the MALDI ionization
22 method are often out of the range of transmission of conventional
23 multipole ion guides.

1 Thus, electric voltages usually applied to the conventional
2 ion guide are used to transmit ions from an entrance end to an exit
3 end. Analyte ions produced in the ion production region pass
4 through a capillary or other ion transfer device to move the ions
5 to a differentially pumped region and enter the ion guide at the
6 entrance end. Through collisions with gas in the ion guide, the
7 kinetic energy of the ions is reduced to thermal energies.
8 Simultaneously, the RF potential on the poles of the ion guide
9 forces ions to the axis of the ion guide. Then, ions migrate
10 through the ion guide toward its exit end, where the ions typically
11 either enter a second ion guide or enter the mass analysis region.

12 Whitehouse also discloses use of two or more ion guides in
13 consecutive vacuum pumping stages to allow different DC and RF
14 values. However, losses in ion transmission efficiency may occur
15 in the region of static voltage lenses between ion guides. For
16 example, a commercially available API/MS instrument manufactured by
17 Hewlett Packard incorporates two skimmers and an ion guide. The
18 drag stage of a conventional turbo pump is used to pump the region
19 between the skimmers. That is, an additional pumping stage/region
20 is added without the addition of an extra turbo pump, and
21 therefore, improved pumping efficiency may be achieved. In this
22 dual skimmer design, there is no ion focusing device between
23 skimmers, therefore ion losses may occur as the gases are pumped

1 away. A second example is demonstrated by a commercially available
2 API/MS instrument manufactured by Finnigan which applies an
3 electrical static lens between capillary and skimmer to focus the
4 ion beam. Due to narrow mass range of the static lens, the
5 instrument may need to scan the voltage to optimize the ion
6 transmission.

7 In addition, the electrode rods of the prior art multipole ion
8 guides described above are positioned in parallel and are equally
9 spaced at a common radius from the centerline of the ion guide.
10 Thus, ions with a m/z ratio falling within the ion guide stability
11 window established by the applied voltages have stable trajectories
12 within the ion guide's internal volume bounded by the parallel,
13 evenly spaced rods. This is true for quadrupoles, hexapoles, etc.
14 For example, FIGs. 3A & 3B depict a prior art hexapole ion guide
15 88. Ion guide 88 shown comprises six conducting rods 86 aligned in
16 parallel and adjacent to one another to form a cylinder-like
17 structure. That is, six parallel conducting rods 86 are evenly
18 spaced from centerline 90 (or axis) of ion guide 88. At either end
19 of ion guide 88 are positioned DC electrodes -- skimmer 84 at
20 entrance end 92 and gate electrode 89 at exit end 94.

21 During operation, DC potentials are applied to each of skimmer
22 84 and gate electrode 89 of multipole ion guide 88 (shown is a
23 hexapole). At skimmer 84 (i.e., entrance end 92 of ion guide 88),

1 ions pass from an ion source region (not shown) through
2 electrically conducting skimmer 84 into the region between the
3 parallel conducting rods 86. In other words, the DC potential
4 applied to skimmer 84 is set such that the ions are focused into
5 ion guide 88. Next, a high voltage RF potential is applied to
6 conducting rods 86 of ion guide 88 to "force" the ions (or focus
7 the ions) to centerline 90 (or axis) of the ion guide. In
8 addition, a collisional gas has been used within such ion guides to
9 collisionally cool the ions therein. Next, the ions will migrate
10 toward exit end 94 of ion guide 88, and at exit end 94 gate
11 electrode 89 is positioned such that a repulsive DC potential may
12 be applied to trap the ions within ion guide 88 until it is time to
13 analyze the ions. On the other hand, when a non-repulsive DC
14 potential is applied to gate electrode 89, the ions may pass freely
15 out of ion guide 88 and into a mass analyzer.

16 In sum, previous ion guides (e.g., quadrupoles, hexapoles,
17 etc.) have comprised parallel conducting rods evenly spaced from a
18 centerline, having DC electrodes positioned at their entrance and
19 exit ends, and high voltage RF and DC potentials are applied
20 thereto to focus, transmit, and/or trap ions. It has been observed
21 that such ion guides are limited in their applications.
22 Specifically, such conventional ion guides may only accept ions
23 from a single ion production means and changing from one ion

1 production means to another is cumbersome and time consuming. In
2 addition, prior art ion guides are often inadequate for
3 transmission of ions produced by the MALDI method, as these ions
4 are often of a m/z range out of the range for which the ion guides
5 are capable. Yet another disadvantage of prior art ion guides is
6 their limited use for mass selection and performing chemical
7 reactions. As discussed below, the ion guide of the present
8 invention overcomes these limitations and/or deficiencies in
9 conventional ion guides.
10

11 SUMMARY OF THE INVENTION

12 The present invention provides an ion guide for use in a mass
13 spectrometer to facilitate the transmission of ions from an
14 elevated pressure ion production region to a reduced pressure ion
15 analysis region. It is one aspect of the invention to utilize
16 multiple ion production means simultaneously to transmit ions into
17 an analyzer. It is another aspect of the invention that
18 embodiments can be interfaced to atmospheric pressure ion sources,
19 including Electrospray (ESI) and electron ionization/chemical
20 ionization (EI/CI). Embodiments of the present invention can be
21 configured in any variety of hyphenated or non-hyphenated analyzer.

22 The invention, as described below, includes a number of
23 embodiments. For instance, the invention can be applied to

1 multipole ion guides with any number of poles, and any geometry.
2 It can utilize multiple ion production means of many different
3 types at the same time, and does not even need to accept ions
4 directly from the ion production means. Also, the analyzer may be
5 any of a variety of hyphenated or non-hyphenated analyzers. The
6 ion guide is positioned between the ion production means and the
7 mass analyzer. However, the ion guide does not need to accept ions
8 directly from the ion production means. In another embodiment of
9 the invention, ions may pass through some other device before
10 entering the ion guide. For example, ions might be produced by an
11 ESI ion production means and be analyzed by ion mobility
12 spectroscopy before entering the ion guide. In the preferred
13 embodiment of the invention as shown in FIG. 6, the ion guide
14 serves as an efficient means for transferring ions through one or
15 more pumping vacuum stages between one or more ion production means
16 and the mass analyzer.

17 In the preferred embodiment of the invention, though, the ion
18 guide need not be planar in cross section as shown in FIG. 4B.
19 Rather, the rods could be arranged to form arcs, or any other
20 useful geometry. Also, the rods could be assembled as a metal
21 deposition (e.g., a vapor deposition) on the insulator. For
22 example, rods might be formed as a gold vapor deposit on two
23 substantially planar ceramic plates. In such a preferred

embodiment, the ceramic plates might be produced, for example, with threaded mounting holes such that the plates can be mounted adjacent to one another in an instrument. The ceramic plates might also have vent holes for allowing gas within the ion guide to pass out of the ion guide and into a pump.

As shown in FIG. 5, it is possible to use the ion guide of the present invention with any number of ion production means (either all being the same type of ion production means or each being a different type of ion production means) including Electrospray 39, EI/CI 40 and MALDI 38. Apertures perpendicular to the axis of the ion guide - i.e. the axis of the rods - are used to pass laser light 400 to the MALDI target 38, and subsequently, the MALDI produced ions from the target 38 to the ion guide 30. A multitude of ion production means could be used simultaneously with the present invention.

The analyzer which accepts ions from the ion guide may also be of a variety of analyzers. These may be hyphenated or non-hyphenated analyzers -- e.g., a time-of-flight mass analyzer (TOFMS), a quadrupole, a quadrupole ion trap, a Fourier transform ion cyclotron resonance mass analyzer (FT-ICRMS), or an ion mobility spectrometer (IMS).

The multipole ion guide is configured to perform many functions including, but not limited to m/z selection, trapping and

1 subsequent ion fragmentation using collision induced dissociation
2 (CID) within the multipole ion guide. Ion selection by m/z is
3 possible by adjusting the DC and RF potentials and the RF frequency
4 on the rods. Gas phase chemical reactions can also be carried out
5 in the invention described. For example, ESI ions may be trapped
6 in the ion guide, and then neutral reactant gas leaked into the
7 guide.

8 In the present invention, multipole ion guides are configured
9 so that ions from a multitude of ion production means can
10 simultaneously be introduced into a single ion guide and
11 transmitted into an analyzer. The ion guide described here can be
12 configured with four (quadrupole), six (hexapole), eight (octapole)
13 or more rods or poles. It is not required that there be a specific
14 entrance point. Rather, there can be a multitude of entrances.
15 Because the present invention allows for a multitude of entrances,
16 a multitude of ion production means can be used simultaneously.

17 Other objects, features, and characteristics of the present
18 invention, as well as the methods of operation and functions of the
19 related elements of the structure, and the combination of parts and
20 economies of manufacture, will become more apparent upon
21 consideration of the following detailed description with reference
22 to the accompanying drawings, all of which form a part of this
23 specification.

1
2 BRIEF DESCRIPTION OF THE DRAWINGS

3 A further understanding of the present invention can be
4 obtained by reference to a preferred embodiment set forth in the
5 illustrations of the accompanying drawings. Although the
6 illustrated embodiment is merely exemplary of systems for carrying
7 out the present invention, both the organization and method of
8 operation of the invention, in general, together with further
9 objectives and advantages thereof, may be more easily understood by
10 reference to the drawings and the following description. The
11 drawings are not intended to limit the scope of this invention,
12 which is set forth with particularity in the claims as appended or
13 as subsequently amended, but merely to clarify and exemplify the
14 invention.

15 For a more complete understanding of the present invention,
16 reference is now made to the following drawings in which:

17 FIG. 1 depicts a prior art mass spectrometer using an ESI ion
18 source;

19 FIG. 2 shows a prior art four vacuum stage ES/MS quadrupole
20 mass spectrometer having a multipole ion guide according to
21 Whitehouse et al. U.S. Pat. No. 5,652,427;

22 FIG. 3A depicts a prior art hexapole ion guide;

23 FIG. 3B shows a cross-sectional view at line A-A of the prior

1 art hexapole shown in FIG. 3A;

2 FIG. 4A shows the preferred embodiment of the multipole ion
3 guide according to the present invention;

4 FIG. 4B shows a cross-sectional view at line B-B of the
5 multipole ion guide shown in FIG. 4A;

6 FIG. 4C shows a top plan view of the multipole ion guide shown
7 in FIG. 4A;

8 FIG. 5A depicts an alternate embodiment of the multipole ion
9 guide of the present invention configured for use with a plurality
10 of ion production means (e.g., EI/CI, ESI, MALDI, etc.);

11 FIG. 5B shows a cross-sectional view at line C-C of the
12 multipole ion guide shown in FIG. 5A;

13 FIG. 5C shows a top plan view of the multipole ion guide shown
14 in FIG. 5A;

15 FIG. 6 shows an internal side view of a multipole ion guide
16 according to co-pending application ser. no. 09/636,321;

17 FIG. 7 is a schematic representation of an internal side view
18 of the preferred embodiment of the RF-DC ion guide assembly
19 according to the present invention as it is incorporated into the
20 multiple stage pumping region of a mass spectrometer; and

21 FIG. 8 shows a simulation of an ion trajectory under certain
22 conditions in an RF-DC ion guide according to the present
23 invention.

1 DETAILED DESCRIPTION OF A PREFERRED EMBODIMENT

2 As required, a detailed illustrative embodiment of the
3 present invention is disclosed herein. However, techniques,
4 systems and operating structures in accordance with the present
5 invention may be embodied in a wide variety of forms and modes,
6 some of which may be quite different from those in the disclosed
7 embodiment. Consequently, the specific structural and functional
8 details disclosed herein are merely representative, yet in that
9 regard, they are deemed to afford the best embodiment for
10 purposes of disclosure and to provide a basis for the claims
11 herein which define the scope of the present invention. The
12 following presents a detailed description of a preferred
13 embodiment (as well as some alternative embodiments) of the
14 present invention.

15 Referring first to FIGs. 4A-4C, shown is the preferred
16 embodiment of the multipole RF-DC ion guide according to the
17 present invention. As depicted, multipole ion guide 100
18 preferably comprises six pairs of parallel conducting rods 102,
19 capping electrodes 104 & 105, and gate electrode 108. Of course,
20 any number of pairs of parallel conducting rods 102 may be used
21 (e.g., 3,4,5,6, etc.). As shown, each pair of conducting rods
22 102 are preferably arranged such that they are equally spaced
23 from one another (or parallel and equidistant from a central long

1 axis). In an alternative embodiment, conducting rods 100 may be
2 arranged in parallel, but not equally spaced from one another.
3 In yet another alternate embodiment, the pairs of conducting rods
4 102 may be positioned such that rods 102 form arcs (i.e., the
5 spacing between rods 102 in a given pair is greater for rods 102
6 in the center of ion guide 100 than rods 102 at its upper and
7 lower edges). Preferably, rods 102 all have different lengths
8 such that at one end of the ion guide 100 all of rods 102 end
9 approximately in a single plane enabling ion guide 100 to be
10 "capped" at this end by a planar (or flat) end capping electrode
11 108.

12 Similarly, ion guide 100 is capped longitudinally on its top
13 and bottom by capping electrodes 104 and 105, respectively.
14 Again, capping electrodes 104 and 105 are substantially planar
15 (or flat) conductive electrodes, but because conducting rods 102
16 are preferably of different lengths, having a first end
17 approximately in a single plane, ion guide 100 preferably has
18 conducting rods 102 forming a second end not in a single plane.
19 That is, conducting rods 102 at the center of ion guide 100 are
20 preferably longest, with conducting rods 102 progressively
21 getting shorter towards the top and bottom edges of ion guide
22 100. Preferably, conducting rods 102 are of such lengths that
23 when positioned in parallel, a side view of ion guide 100 depicts

1 the second end of rods 102 forming a generally semicircular
2 shape. In such an embodiment, top and bottom capping electrode
3 104 has a generally curved portion which conforms to the shape of
4 the second end of ion guide 100 formed by conducting rods 102.
5 Of course, top and bottom capping electrode 104 is such that
6 opening 106 remains at the second end of ion guide 100 for
7 introduction of the ions into ion guide 100. Specifically, the
8 entrance end of ion guide 100, top and bottom capping electrode
9 104 extends continuously around the second end of conducting rods
10 102.

11 For example, sample ions enter ion guide 100 through
12 aperture (or opening) 106 and exit ion guide 100 through exit
13 electrode 108. Preferably, high voltage RF potentials are
14 applied between conducting rods 102, with top and bottom capping
15 electrode 104 being held at a repulsive DC potential to "force"
16 the ions toward the center of ion guide 100. As shown in FIG. 8,
17 which depicts a simulated ion trajectory in an ion guide
18 according to the present invention, application of optimum
19 potentials to capping electrodes 222 and conducting rods 224
20 focus ions to the center 230 of ion guide 225. In the simulation
21 depicted, the following parameters were used: conducting rods 224
22 were 0.9 mm in diameter (234), vertically spaced (232) 0.75 mm
23 apart and horizontally spaced (228) 3.0 mm apart; a potential of

1 10 volts was applied to capping electrodes 222; and a potential
2 of 600 volts (peak to peak) was applied to conducting rods 224.
3 As shown, the net effect of the application of these potentials
4 on capping electrodes 222 and conducting rods 224 is the creation
5 of electric fields (depicted as equipotential lines 226) which
6 force the ions toward the center 230 of ion guide 225. Under
7 these conditions, the energy of the ions at center 230 of ion
8 guide 225 is defined as 100 Da/q or 1 eV. In addition, the
9 potential established at center 230 is 0.18 volts while the
10 potential at equipotential line 226 nearest center 230 is 0.9
11 volts, thereby establishing a net effect of forcing the ions to
12 the region having a lower potential -- center 230 of ion guide
13 225.

14 Turning next to FIG. 4B, shown is a cross-sectional view at
15 line A-A of ion guide 100. In particular, shown in FIG. 4B is
16 the preferred parallel arrangement of conducting rods 102. As
17 depicted, each pair of conducting rods 102 are preferably equally
18 spaced from one another, and the rods in each pair are spaced
19 apart the same distance as each other pair. Optionally, however,
20 the rods in each pair may be spaced apart at varying distances as
21 each other pair, thereby forming a generally curved (or arched)
22 structure (not shown). Also, FIG. 4B demonstrates the continuous
23 structure of capping electrode 104, only having opening 106 to

1 allow introduction of the ions into ion guide 100.

2 Next, FIG. 4C shows a top plan view of ion guide 100. As
3 shown in FIG. 4C, ion guide 100 has at its exit end gate
4 electrode 108, gate electrode 108 preferably comprising an
5 opening (or aperture) for allowing ions to pass out of ion guide
6 100 when gate electrode 108 is deenergized. Alternatively, gate
7 electrode 108 may comprise a grid electrode. Preferably, gate
8 electrode 108 comprises two parallel electrodes spaced apart such
9 that ions may pass there through when the electrodes are
10 deenergized. Alternatively, gate electrode 108 may be a planar
11 electrode at a repulsive DC potential until such time that the
12 ions are to be released from ion guide 100 to the next stage of
13 the mass spectrometer (i.e., the mass analyzer). Repulsion of
14 the ions from the DC potentials on top and bottom capping
15 electrode 104 and gate electrodes 108 in conjunction with the RF
16 potential applied to conducting rods 102 may be used to trap ions
17 within ion guide 100 for any length of time (i.e., to allow for
18 sufficient cooling of the ions, to better focus the ions, etc.)
19 prior to entering the mass analyzer.

20 Referring next to FIGs. 5A-C, shown is an alternate
21 embodiment of the present invention configured for use with a
22 plurality of ion production means, either separately or
23 simultaneously. Specifically, depicted is ion guide 120

1 incorporating ESI ion production means 118, EI/CI ion production
2 means 112, and MALDI ion production means 116 simultaneously. As
3 depicted, multipole ion guide 120 preferably comprises six pairs
4 of parallel conducting rods 132, capping electrodes 130, and gate
5 electrode 134. Of course, any number of pairs of parallel
6 conducting rods 132 may be used (e.g., 3, 4, 5, 6, etc.). As
7 shown, conducting rods 132 are preferably arranged such that they
8 are equally spaced from one another (or parallel and equidistant
9 from a central long axis). In an alternative embodiment,
10 conducting rods 132 may be arranged in parallel, but not equally
11 spaced from one another. In yet another alternate embodiment,
12 the pairs of conducting rods 132 may be positioned such that rods
13 132 form arcs (i.e., the spacing between rods 132 in a given pair
14 is greater for rods 132 in the center of ion guide 120 than rods
15 132 at its upper and lower edges). Preferably, rods 132 all have
16 different lengths such that at one end of the ion guide 120 all
17 of rods 132 end approximately in a single plane enabling ion
18 guide 120 to be "capped" at this end by a planar (or flat) end
19 capping electrode 134. Similarly, ion guide 120 is capped
20 longitudinally on its top and bottom by capping electrodes 130.
21 Again, capping electrodes 130 are substantially planar (or flat)
22 conductive electrodes, but because conducting rods 132 are
23 preferably of different lengths, having a first end approximately

1 in a single plane, ion guide 120 preferably has conducting rods
2 132 forming a second end not in a single plane. That is,
3 conducting rods 132 at the center of ion guide 120 are preferably
4 longest, with conducting rods 132 progressively getting shorter
5 towards the top and bottom edges of ion guide 120. Preferably,
6 conducting rods 132 are of such lengths that when positioned in
7 parallel, a side view of ion guide 120 depicts the second end of
8 rods 132 forming a generally semicircular shape. In such an
9 embodiment, top and bottom capping electrode 130 has a generally
10 curved portion which conforms to the shape of the second end of
11 ion guide 120 formed by conducting rods 132. Of course, top and
12 bottom capping electrode 130 is such that opening 122 remains at
13 the second end of ion guide 120 for introduction of the ions into
14 ion guide 120. Specifically, the entrance end of ion guide 120,
15 top and bottom capping electrode 130 extends continuously around
16 the second end of conducting rods 132.

17 For example, sample ions enter ion guide 120 through
18 aperture (or opening) 122 and exit ion guide 120 through exit
19 electrode 134. Preferably, high voltage RF potentials are
20 applied to conducting rods 132, with top and bottom capping
21 electrode 130 being held at a repulsive DC potential to "force"
22 the ions toward the center of ion guide 120.

23 First, regarding ESI ion production means 118, the ions

1 enter ion guide 120 through aperture 122 in capping electrode
2 130. As with conventional ESI, sample solution is sprayed from a
3 sprayer (not shown) such that a spray of fine droplets of sample
4 solution exits a spray needle (not shown) of the sprayer. Due to
5 an electrical potential between the spray needle and the entrance
6 end (not shown) of capillary 118, the fine droplets of sample
7 solution are ionized. The formed analyte ions then enter
8 capillary 118 through an opening in the entrance end, and the
9 ions are transported through a channel within capillary 118 to
10 exit end 117 of capillary 118. Upon exiting capillary 118, the
11 ions 119 may enter ion guide 120 through aperture 122. As
12 described above, a flow of neutral gas may be used to aid or
13 guide the ions into ion guide 120 through aperture 122.
14 Optionally, as shown in FIG. 7, a pre-multipole ion guide (not
15 shown in FIG. 5A) may be positioned between capillary 118 and ion
16 guide 120.

17 Second, with respect to EI/CI ion production means 112,
18 sample ions may enter ion guide 120 through aperture 124. As
19 shown, aperture 124 is positioned at an angle with respect to
20 conducting rods 132 of ion guide 120. Optionally, EI/CI source
21 may be positioned at aperture 122 in place of ESI source 118, or
22 alternatively at aperture 126 in place of the MALDI laser 114.

23 Third, regarding MALDI ion production means 114/116, ions

1 are introduced into ion guide 120 through aperture 128 when MALDI
2 sample 116 is struck by MALDI Laser 117. The laser light passes
3 through ion guide 120 after entering at aperture 126 and exits
4 through aperture 128. Upon exiting aperture 128, laser beam 114
5 strikes MALDI sample surface 116 thereby generating sample ions
6 which pass into ion guide 120 through aperture 128.

7 With each of these ionization methods, capping electrode 130
8 maintains a repulsive DC potential, as does gate electrode 137 at
9 the exit end of ion guide 120. Of course, it is consistent with
10 the invention that other types of ionization methods may be used
11 (e.g., atmospheric pressure chemical ionization, plasma
12 desorption, glow discharge, secondary ionization, fast atom
13 bombardment, etc.). Also, in accordance with the invention, ions
14 need not be accepted directly from an ion production means.
15 Rather, ions may pass through some other device before entering
16 the ion guide. For example, ions might be produced by an ESI
17 source and be analyzed by ion mobility spectroscopy before
18 entering the ion guide. Alternatively, ions may pass through a
19 capillary device before entering the ion guide.

20 Turning next to FIG. 5B, shown is a cross-sectional view at
21 line B-B of ion guide 120. As shown in FIG. 5B, the six pairs of
22 conducting rods are aligned in parallel and adjacent to one
23 another such that the first rod of all pairs of rods 132 lie in a

1 first plane, while the second rod of all pairs of rods 132 lie in
2 a second plane which is parallel to the first plane.
3 Alternatively, conducting rods 132 may not lie in a single plane,
4 but rather may be positioned in an arc-like formation, an angled
5 formation, or some other desired configuration. In addition, as
6 shown in FIG. 5B, capping electrode 130 includes circular opening
7 122 to provide for the introduction of ions into guide 120 from
8 source 118. Similarly, openings 124, 126 and 128 are preferably
9 circular apertures to provide for the introduction of sample ions
10 from EI/CI ion production means 112, laser beam 114 to ionize
11 samples on MALDI sample 116, and sample ions from MALDI sample
12 116, respectively. Alternatively, openings 122, 124, 126 and 128
13 may be any shape (i.e., square, triangular, rectangular,
14 hexagonal, etc.)

15 An alternate embodiment (not shown) of ion guide 120
16 comprises multiple capping electrodes. That is, capping
17 electrode 130 as shown in FIG. 5A may comprise five parts, with a
18 space or gap between each part. These spaces provide the same
19 functions as openings 122, 124, 126 and 128 in FIG. 5A. Of
20 course, this embodiment would require that each part of the
21 capping electrode be attached to a power source such that the
22 appropriate potentials may be applied thereto. In addition,
23 capping electrode 130 may comprise fewer than five parts -- for

1 example, it may comprise a top electrode, a bottom electrode, and
2 an end electrode. In this embodiment, openings 126 and 128 are
3 formed from the space or gap between the top electrode and end
4 electrode, respectively. Openings 122 and 124 may then comprise
5 circular (or some other shape) apertures. Again, each part
6 (i.e., top, bottom and end) of the capping electrode must be
7 connected to a power supply for application of the appropriate
8 potentials.

9 Next, as with FIG. 4C above, FIG. 5C shows a top plan view
10 of ion guide 120. Ion guide 120 has at its exit end gate
11 electrode 134, gate electrode 134 preferably comprising an
12 opening (or aperture) for allowing ions to pass out of ion guide
13 120 when gate electrode 134 is deenergized. Alternatively, gate
14 electrode 134 may comprise a grid electrode. Preferably, gate
15 electrode 134 is held comprising two parallel electrodes spaced
16 apart such that ions may pass there through when the electrodes
17 are deenergized. Alternatively, gate electrode 134 may be a
18 planar electrode at a repulsive DC potential until such time that
19 the ions are to be released from ion guide 120 to the next stage
20 of the mass spectrometer (e.g., the mass analyzer). Repulsion of
21 the ions from the DC potentials on top and bottom capping
22 electrode 130 and gate electrodes 134 in conjunction with the RF
23 potential applied to conducting rods 132 may be used to trap ions

1 within ion guide 120 for any length of time (i.e., to allow for
2 sufficient cooling of the ions, to better focus the ions, etc.)
3 prior to entering the mass analyzer.

4 Turning now to FIG. 6, shown is multipole ion guide assembly
5 140, as described in co-pending application ser. no. 09/636,321.
6 As depicted, multipole ion guide assembly 140 disclosed therein
7 comprises skimmers 148 & 150, pre-multipole 144, multipole 146,
8 and exit electrodes 156. As shown, multipole ion guide assembly
9 140 is positioned such that it may transfer ions from a first
10 pumping stage 145 to mass analysis region 155, across one or more
11 intermediate differential pumping stages.

12 During operation, ions may be generated from an API source
13 (e.g., ESI or APCI) (not shown), and are introduced into first
14 differential pumping stage 145 through an ion transport device
15 such as a capillary. First pumping stage 145 may be pumped to a
16 pressure lower than atmospheric pressure, for example, to a
17 pressure of approximately 1-2 mbar. The transported ions in
18 first pumping stage 145 are directed by an electric field into
19 orifice 152 of first skimmer 150 and into multipole ion guide
20 assembly 140. The electric field may be generated by application
21 of a potential difference across , for example, a capillary's
22 exit end and first skimmer 150. This electric field is applied
23 such that the ions are directed toward orifice 152 of first

1 skimmer 150, while neutral gas particles are pumped away.
2 Optionally, this electric field may be varied depending on the
3 desired result, the size of the ions being directed, the distance
4 between a capillary exit end and first skimmer 150, etc.
5 Alternatively, it is envisioned that in certain situations better
6 results may be obtained without application of an electric field
7 across the capillary exit end and first skimmer 150. Optionally,
8 o-ring seals 158 may be used to provide a lateral seal between
9 pressure regions.

10 The ions which pass through orifice 152 of skimmer 150 then
11 enter a second differential pumping stage, which is further
12 pumped by a vacuum pump (e.g., a turbo molecular drag pump).
13 This second pumping stage may be pumped and maintained at a
14 pressure in the range from 1×10^{-2} mbar to 1×10^{-1} mbar. At this
15 point, the surviving ions enter pre-multipole 144, which may be
16 operated as an RF only ion guide, wherein the ions are further
17 separated from any neutral gas molecules. Pre-multipole 144 may
18 comprise a plurality of electrode rods, each having a potential
19 applied thereto such that the resulting electric field "pushes"
20 or forces the ions toward a central axis as the ions continue to
21 move through pre-multipole 144 toward a second skimmer 148 (which
22 leads to yet another pumping stage). The ions then pass through
23 second skimmer 148, while the neutral gas molecules, which are

1 not affected by the electrical field, are pumped away. In one
2 configuration, pre-multipole 144 is positioned between first
3 skimmer 150 and second skimmer 148, and is located entirely in a
4 second differential pumping stage. Of course, alternative
5 configurations may be used. For example, pre-multipole 144 may
6 be positioned to cross from one pumping stage to another, one or
7 both skimmers may be removed, or one or both skimmers may be
8 replaced with focusing lenses (e.g., Einzel lenses, etc.).

9
10 As the ions pass through second skimmer 148, they enter yet
11 another (third) pumping stage and multipole 146. This third
12 pumping stage may be pumped to and maintained at a pressure in
13 the range from 1×10^{-3} mbar to 1×10^{-2} mbar. At this point, the
14 surviving ions enter multipole 146, which may be operated as an
15 RF only ion guide, wherein the ions are further separated from
16 any neutral gas molecules. As described in co-pending
17 application ser. no. 09/636,321, multipole 146 may comprise a
18 plurality of electrodes, each having an electric potential
19 applied thereto such that the resulting electric field "pushes"
20 or forces the ions toward a central axis of multipole 146.
21 Again, application of the electric field may separate the ions
22 from other neutral gas molecules present (which are pumped away
23 because they are not affected by the electrical field). That is,
neutral gas molecules will be continuously pumped away by the

1 connected pump (not shown) (e.g., a turbo molecular drag pump).
2 In addition, the introduction or presence of collisional gas into
3 the third pumping stage results in the collisional cooling of the
4 ions within multipole 146 as the ions are being "guided"
5 therethrough. The cooled ions then pass through exit electrodes
6 156 as they are introduced into mass analysis region 155 for
7 subsequent mass analysis. Mass analysis region 155 may comprise
8 any of a number of mass analysis devices, including but not
9 limited to time-of-flight (TOF), quadrupole (Q), Fourier
10 transform ion cyclotron resonance (FTICR), magnetic (B),
11 electrostatic (E) or quadrupole ion trap analyzers.

12 In an embodiment of the multipole ion guide assembly 140 (as
13 described in co-pending application ser. no. 09/636,321,
14 multipole 146 is positioned between second skimmer 148 and exit
15 electrodes 156 (which lead to mass analysis stage 155), with
16 multipole 146 being positioned within the third pumping stage.
17 Of course, alternate configurations are described, such as,
18 multipole 146 being positioned across multiple pumping stages,
19 skimmer 148 or exit electrodes 156 being removed or replaced by
20 other elements such as focusing lenses (e.g., Einzel lenses,
21 etc.).

22 In addition, the preferred embodiment of multipole ion guide
23 assembly 140 (as set forth in co-pending application ser. no.

1 09/636,321) includes pre-multipole 144 positioned between first
2 and second skimmers (150 & 148, respectively) to separate the
3 ions from any existing neutral gas molecules prior to the ions
4 entering multipole 146. In addition, pre-multipole 144 may focus
5 ions onto the center of second skimmer 148 while the neutral gas
6 molecules are pumped away. Efficient differential pumping in the
7 pumping stages allows multipole 146 (the main ion guide) to be in
8 a pressure region having a pressure which is both low enough for
9 ion trapping and high enough for collisional cooling. Multipole
10 ion guide assembly 140 may be used in applications requiring
11 either ion trapping (for a specific period of time), ion
12 selecting, ion fragmenting, etc. For instance, if the pressure
13 in the region containing multipole 146 is too high, ions may be
14 scattered or fragmented. In a single skimmer system, the effects
15 of this scattering or fragmenting are difficult to manage. The
16 presence of more than one skimmer along with short pre-multipole
17 144 minimizes scattering and fragmentation of the sample ions.

18 Also as shown, multipole ion guide assembly 140 may comprise
19 housing 142 in which first skimmer 150, second skimmer 148, pre-
20 multipole 144, multipole 146, and exit electrodes 156 are all
21 secured in longitudinal alignment. These ion optic elements are
22 all maintained in longitudinal alignment with each other such
23 that ions may be transported on a single axis through each

1 optical component of multipole ion guide assembly 140 from the
2 ion production region (or first pumping region 145) to the mass
3 analyzer in mass analysis region 155. Housing 142 may be made
4 from any rigid and durable material, such as aluminum.

5 Within housing 142, skimmers 150 and 148, pre-multipole 144,
6 multipole 146 and exit electrodes 156 all may be secured by
7 insulating holders. These insulating holders may provide
8 electrical insulation for each component from housing 142, as
9 well as from each other. In addition, these insulating holders
10 secure skimmers 150, 148, pre-multipole 144, multipole 146 and
11 exit electrodes 156 all in longitudinal alignment within housing
12 142.

13 During operation of multipole ion guide assembly 140, as
14 shown in FIG. 6, sample ions are first introduced through orifice
15 152 of skimmer 150 (as discussed above) and enter a first pumping
16 stage and pre-multipole 144. While, in pre-multipole 144, the
17 ions are separated from any existing neutral gas molecules, and
18 are transported longitudinally therethrough. That is, an
19 electric field, which is generated through the application of
20 potentials to the rods of pre-multipole 144, forces the ions
21 towards the center axis of pre-multipole 144 as the ions move
22 longitudinally therethrough. The electric field has no effect on
23 the neutral gas molecules, such that substantially all of these

1 molecules are not transported through or directed through pre-
2 multipole 144.

3 Once transported through pre-multipole 144, the sample ions
4 are introduced through orifice 154 of skimmer 148 (as discussed
5 above) and into a second pumping stage and multipole 146. While
6 in multipole 146, the ions are further separated from any
7 existing neutral gas molecules, are trapped, collisionally
8 cooled, selected, fragmented, scattered, etc. (as discussed
9 above), and are transported longitudinally therethrough. At the
10 exit end of multipole 146, the selected (or fragmented, etc.)
11 sample ions pass through exit electrodes 156 where the ions may
12 be accelerated into a mass analyzer for subsequent analysis.

13 Regarding multipole ion guide assembly 140 shown in FIG. 6,
14 it is important that the insulating holders and housing 142
15 maintain the electrical independence of skimmers 150 & 148, pre-
16 multipole 144, multipole 146, and exit electrodes 156, even
17 though such components are secured in longitudinal alignment
18 within housing 142. For instance, individual components, and
19 also individual elements within the individual components, may
20 require application of separate and/or different electrical
21 potentials for optimum performance. Therefore, it is important
22 that the electrical independence of each component is maintained.
23 However, in other embodiments, certain components (i.e., skimmer

1 150 and skimmer 148) of multipole ion guide assembly 140 may be
2 in electrical contact with one another such that the same
3 electric potentials may be applied to each through a single
4 connection to a power source.

5 Referring next to FIG. 7, depicted is multipole ion guide
6 assembly 200, which incorporates the preferred embodiment of ion
7 guide 193 according to the invention, as it is incorporated into
8 the multiple stage pumping region of a mass spectrometer. Such a
9 system includes multipole ion guide assembly 200, capillary 182,
10 first, second and third differential pumping stages 204, 206 &
11 208, each of which being connected to a vacuum pump (e.g.,
12 roughing pump 218 and a turbo pump having drag stage 219 & main
13 stage 217, respectively, and mass analysis region 202, which is
14 connected to a second turbo pump 220. Alternatively, a single
15 pump or pumping system may be used in accordance with the
16 invention. Also, shown is ion guide 193 configured for use with
17 a conventional mass spectrometer using an ESI ion production
18 means. Specifically, ions are produced from a sample material
19 and a sample solution enters ionization region 216 through a
20 spray needle, at the end of which the sample solution is formed
21 into a spray of fine droplets. This spray is formed as a result
22 of an electrostatic field applied between the spray needle and
23 the sampling orifice of capillary 182. Alternatively, the

1 sampling orifice may be an aperture or other similar inlet
2 leading into the vacuum regions of the mass spectrometer. Due to
3 the applied electrostatic field, electrosprayed droplets
4 evaporate while in the ionization region thereby producing gas
5 phase analyte ions which enter the sampling orifice of capillary
6 182. Optionally, heated drying gas may be used to assist the
7 evaporation of the droplets and passage of ions into capillary
8 182. Thus, some of the analyte ions are carried with the gas
9 from the ionization region through capillary 182 and into first
10 vacuum region 204 of the mass spectrometer.

11 Similar to that described above for FIG. 6, multipole ion
12 guide assembly 200 comprises skimmers 186 & 196, pre-multipole
13 188, RF-DC ion guide 193, and exit electrodes 212. As depicted
14 in FIG. 7, multipole ion guide assembly 200 is positioned such
15 that it may transfer ions from ion source region 216 to mass
16 analysis region 202, across one or more differentially pumped
17 regions of a mass spectrometer.

18 During operation, ions may be generated from an API ion
19 production means (e.g., ESI or APCI) (not shown), and are
20 introduced into first differential pumping region 204 through an
21 ion transport device such as a capillary. Alternatively, ions
22 may enter region 204 directly from an ion production means. This
23 first region 204 is preferably pumped to a pressure lower than

1 atmospheric pressure by vacuum pump 218 -- for example, region
2 204 may be pumped to a pressure of approximately 1-2 mbar. Once
3 within region 204, the transported ions are directed by an
4 electric field into orifice 210 of first skimmer 186 and into
5 multipole ion guide assembly 200. The electric field may be
6 generated by application of a potential difference across, for
7 example, capillary exit end 184 and first skimmer 186.

8 Alternatively, the electric field may be generated by application
9 of a potential difference across an ion source (e.g., a spray
10 needle) and first skimmer 186. This electric field may be
11 applied such that the ions are directed toward orifice 210 of
12 first skimmer 186, while neutral gas particles are pumped away.
13 Optionally, this electric field may be varied depending on the
14 desired result, the size of the ions being directed, the distance
15 between capillary exit 184 (or some other element) and first
16 skimmer 186, etc. Alternatively, it is envisioned that in
17 certain situations better results may be obtained without
18 application of the electric field across capillary exit 184 and
19 first skimmer 186.

20 The ions that pass through first skimmer 186 then enter
21 second differential pumping region 206, which is further pumped
22 by vacuum pump 219 (e.g., a turbo molecular drag pump) to a lower
23 pressure region, preferably, in the range from 1×10^{-2} mbar to

1 1×10^{-1} mbar. Here, the surviving ions may enter pre-multipole
2 188, preferably operated as an RF only ion guide, wherein the
3 ions are further separated from any neutral gas molecules. The
4 preferred embodiment of pre-multipole 188 is described fully in
5 co-pending application ser. no. 09/636,321, which is herein
6 incorporated by reference. Generally, though, pre-multipole 188
7 comprises a plurality of electrode rods, each having a potential
8 applied thereto such that the resulting electric field "pushes"
9 or "forces" the ions toward a central axis as the ions continue
10 to move through pre-multipole 188 toward orifice 198 of skimmer
11 196 (which leads to yet another pumping region).

12 The ions then pass through second skimmer 196, while the
13 neutral gas molecules, which are not affected by the electrical
14 field, are pumped away. In the preferred embodiment, pre-
15 multipole 188 is positioned between first skimmer 186 and second
16 skimmer 196, and is located entirely in first differential
17 pumping region 204. Of course, alternative arrangements may be
18 used. For example, pre-multipole 188 may be positioned to cross
19 from one pumping stage to another (i.e., from first pumping
20 region 204 into second pumping region 206), one or both skimmers
21 may be removed, or one or both skimmers may be replaced with
22 focusing lenses (e.g., Einzel lenses, etc.).

23 Once through orifice 198 of second skimmer 196, the ions

1 preferably enter third pumping region 208 where they also enter
2 RF-DC ion guide 193. Preferably, this third pumping region 208
3 is pumped to and maintained at a pressure in the range from 1×10^{-3}
4 mbar to 1×10^{-2} mbar. Here, the surviving ions enter ion guide
5 193, preferably operated as an RF-DC ion guide, wherein the ions
6 are further separated from any neutral gas molecules. As
7 described herein above with respect to FIGs. 4A-4C, ion guide 193
8 preferably comprises six pairs of parallel conducting rods 194
9 (although only four pairs are shown in FIG. 7), capping
10 electrodes 192, and gate electrodes 212. Of course, any number
11 of pairs of parallel conducting rods may be used (e.g., 3, 4, 5,
12 6, etc.). As specifically shown in FIG. 4B, each pair of
13 conducting rods 194 is preferably arranged such that it is
14 equally spaced from its immediately adjacent pair (and parallel
15 and equidistant from a central long axis). In an alternative
16 embodiment, conducting rods 194 may be arranged in parallel, but
17 not equally spaced from one another. In yet another alternate
18 embodiment, the pairs of conducting rods 194 may be positioned
19 such that rods 194 form arcs (i.e., the spacing between rods 194
20 in a given pair is greater for rods 194 in the center of ion
21 guide 193 than rods 194 at its upper and lower edges).
22 Preferably, pairs of conducting rods 194 all have different
23 lengths such that at one end of the ion guide 193 (i.e., at its

1 exit end) all of rods 194 end approximately in a single plane
2 enabling ion guide 193 to be "capped" at this end by a planar (or
3 flat) exit electrode 212. Similarly, ion guide 193 is "capped"
4 longitudinally on its top and bottom by capping electrodes 192.
5 Again, capping electrodes 192 are substantially planar (or flat)
6 conductive electrodes. Because conducting rods 194 are
7 preferably of different lengths, having a first end approximately
8 in a single plane, ion guide 193 preferably has conducting rods
9 194 forming a second end which is not in a single plane. That
10 is, conducting rods 194 at the center of ion guide 193 are
11 preferably longest, with conducting rods 194 being shorter
12 towards the top and bottom edges of ion guide 193.

13 Preferably, conducting rods 194 are of such lengths that
14 when positioned in parallel, a side view of ion guide 193 (as
15 shown in FIG. 7) depicts the second end of rods 194 (i.e., at its
16 entrance end) forming a generally angular shape. In such an
17 embodiment, top and bottom capping electrode 192 may be generally
18 bent to conform to the shape of skimmer 196. However, as shown
19 in FIG. 7, capping electrodes may be entirely flat (or planar)
20 and skimmer 196 may be used to "cap" the entrance end of ion
21 guide 193. Alternatively, conducting rods 194 may be of such
22 lengths that when positioned in parallel, a side view of ion
23 guide 193 depicts the second end of rods 194 (i.e., at its

entrance end) forming a generally semicircular shape (see FIG. 5), flat shape, reverse angular shape (i.e., where the central conducting rods 194 are shorter than the upper and lower conducting rods 194), etc. Of course, the top and bottom capping electrodes 192 would be modified accordingly to correspond to the shape of the arrangement of conducting rods 194.

During operation, sample ions enter ion guide 193 through orifice 198 of skimmer 196 and exit ion guide 193 through exit electrodes 212. Preferably, high voltage RF potentials are applied between conducting rods 194, with top and bottom capping electrode 192 being held at a repulsive DC potential to "force" the ions toward the central axis (i.e., the longitudinal axis) of ion guide 193. Application of the electric field separates the ions from other neutral gas molecules present (which are pumped away because they are not affected by the electrical field). That is, neutral gas molecules will be continuously pumped away by vacuum pump 217 (not shown) (e.g., a turbo molecular drag pump). In addition, the introduction (or presence) of collisional gas in third pumping region 208 (i.e., where ion guide 193 is located) results in the collisional cooling of the ions within ion guide 193 as the ions are being "guided" therethrough. The cooled ions then pass through exit electrodes 212 as they are introduced into mass analysis region 202 for

1 subsequent mass analysis. Mass analysis region 202 may comprise
2 any of a number of mass analysis devices, including but not
3 limited to time-of-flight (TOF), quadrupole (Q), Fourier
4 transform ion cyclotron resonance (FTICR), magnetic (B),
5 electrostatic (E), or quadrupole ion trap analyzers.

6 In the preferred embodiment of the invention, ion guide 193
7 is positioned between second skimmer 196 and exit electrodes 212
8 (which lead to mass analysis region 202), with ion guide 193
9 being entirely positioned within a single pumping region (here it
10 is the third region). Of course, alternative configurations may
11 be used, including but not limited to, for example, ion guide 193
12 being positioned across multiple pumping stages, skimmer 196 or
13 exit electrodes 212 being removed or replaced by other elements
14 such as focusing lenses (e.g., Einzel lenses, etc.), etc.

15 As demonstrated in FIG. 7, the preferred embodiment of ion
16 guide 193 is used in multipole ion guide assembly 200, which
17 includes pre-multipole 188 comprising short (e.g., 8-20 mm)
18 electrodes between first and second skimmers (186 & 196,
19 respectively) to separate the ions from any existing neutral gas
20 molecules prior to the ions entering ion guide 193. In addition,
21 pre-multipole 188 may "focus" ions onto orifice 198 of second
22 skimmer 196 while the neutral gas molecules are pumped away.
23 Efficient differential pumping in the pumping regions allows ion

1 guide 193 to be in a pressure region having a pressure which is
2 both low enough for ion trapping and high enough for collisional
3 cooling. Therefore, ion guide 193 according to the present
4 invention may be used in applications requiring either ion
5 trapping (for a specific period of time), ion selecting, ion
6 fragmenting, etc. For instance, if the pressure in the region
7 containing ion guide 193 is too high, ions may be scattered or
8 fragmented. In a single skimmer system, the effects of this
9 scattering or fragmenting are difficult to manage. Conversely,
10 when using ion guide assembly 200, the presence of more than one
11 skimmer along with short pre-multipole 188 minimizes scattering
12 and fragmentation of the sample ions.

13 Also as shown in FIG. 7, multipole ion guide assembly 200
14 comprises housing 190 in which first skimmer 186, second skimmer
15 196, pre-multipole 188, ion guide 193, and exit electrodes 212
16 are all secured in longitudinal alignment. These ion optic
17 elements are all maintained in longitudinal alignment with each
18 other such that ions may be transported on a single axis through
19 each optical component of multipole ion guide assembly 200 from
20 the region 216 (i.e., an ion source region, a first pumping
21 region, etc.) to the mass analyzer in mass analysis region 202.
22 Preferably, housing 190 is made from a rigid and durable
23 material, such as aluminum, although certain other metal or

1 plastic materials may be used. Optionally, o-ring seals 214 may
2 be used to provide a lateral seal between pumping regions 204,
3 206, 208 and 202.

4 Within housing 190, skimmers 186 & 196, pre-multipole 188,
5 multipole 193 and exit electrodes 212 are all preferably secured
6 in longitudinal alignment by insulating holders (not shown).
7 These insulating holders preferably provide electrical insulation
8 for each component from housing 190, as well as from each other.

9 In a preferred operation of multipole ion guide assembly 200
10 as shown in FIG. 7, sample ions are first introduced through
11 orifice 210 of skimmer 186 (as discussed above) into pumping
12 region 204 containing pre-multipole 188. While within pre-
13 multipole 188, the ions are separated from any existing neutral
14 gas molecules, and are transported longitudinally therethrough.
15 That is, an electric field, which is generated through the
16 application of potentials to the rods of pre-multipole 188,
17 forces the ions towards the center axis of pre-multipole 188 as
18 the ions move longitudinally therethrough. The electric field
19 has no effect on the neutral gas molecules, such that
20 substantially all of these molecules are not transported through
21 or directed through pre-multipole 188.

22 After passing through pre-multipole 188, ions are introduced
23 through skimmer 196 (as discussed above) into second pumping

1 region 206 and ion guide 193. As previously described herein
2 regarding FIGs. 4A-4C, while in ion guide 193, the ions are
3 further separated from any existing neutral gas molecules, are
4 trapped, collisionally cooled, selected, fragmented, scattered,
5 etc. (as discussed above), and are transported longitudinally
6 therethrough. At the exit end of ion guide 193, the selected (or
7 fragmented, etc.) sample ions pass through exit electrodes 212
8 where the ions may be accelerated into a mass analyzer for
9 subsequent analysis.

10 In multipole ion guide assembly 200, which incorporates the
11 preferred embodiment of ion guide 193 according to the present
12 invention, as shown in FIG. 7, it is important that the
13 insulating holders and housing 190 maintain the electrical
14 independence of skimmers 186 & 196, pre-multipole 188, ion guide
15 193 and exit electrodes 212, even though such components are
16 secured in longitudinal alignment within housing 190. This is
17 because individual components, and also individual elements
18 within the individual components, may require application of
19 separate and/or different electrical potentials for optimum
20 performance. For example, regarding ion guide 193, different
21 potentials are preferably applied to conducting rods 194 than are
22 applied to capping electrodes 192. Therefore, it is preferred
23 that the electrical independence of each component is maintained.

1 However, in an alternative embodiment certain components (i.e.,
2 skimmer 186 and skimmer 196) of multipole ion guide assembly 200
3 may be in electrical contact with one another such that the same
4 electric potentials may be applied to each with a single
5 connection to a power source.

6 While the present invention has been described with
7 reference to one or more preferred embodiments, such embodiments
8 are merely exemplary and are not intended to be limiting or
9 represent an exhaustive enumeration of all aspects of the
10 invention. The scope of the invention, therefore, shall be
11 defined solely by the following claims. Further, it will be
12 apparent to those of skill in the art that numerous changes may
13 be made in such details without departing from the spirit and the
14 principles of the invention. It should be appreciated that the
15 present invention is capable of being embodied in other forms
16 without departing from its essential characteristics.